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I. Introduction

Antibodies are key effector molecules of the adaptive immune response, playing a central role in host defence against pathogenic organisms and other foreign antigens. These molecules can eliminate infections via different mechanisms, including direct binding and neutralisation of pathogens to prevent infection and facilitate clearance together with other innate immune cells. Through this interplay between the innate and adaptive immune system, the formation of antibody-antigen complexes capture and remove pathogens, neutralise toxins, eliminate infected cels, enhance antigen presentation, and modulate inflammatory responses [1].

These concepts of antigen recognition and immune complex formation extend beyond infectious immunity. They also have direct implications for clinical procedures such as blood transfusion. Incompatible transfusions may lead to widespread antibody-binding and immune complex formation in a recipient, triggering life-threatening haemolytic reactions [2, 3].

It is also imperative to recognise that immune complexes, despite their protective roles, can also give rise to diseases when not effectively removed. Their buildup in tissues can activate the complement system, leading to chronic inflammation. One such classic clinical example is the presence of rheumatoid factors (RF), a group of IgM autoantibodies that bind to and are directed against the Fc fragment of IgG molecules [4].

II. Immune Complexes in Pathogenic Infections

Antibodies are multifunctional glycoproteins that are produced by plasma cells in the body. These molecules are key players of the adaptive immune response against foreign pathogens and antigens. In the human body, there are five classes of antibodies produced and these include IgM, IgG, IgE, IgA, and IgD. During a primary infection, IgM is the first class of antibodies generated. This antibody is a pentameric molecule that binds to the foreign antigen with high avidity. On the other hand, IgG is a monomeric antibody that is the most abundant class of antibody in serum [5]. IgG is mostly produced during a secondary immune response, and is crucial in neutralising pathogens and are crucial for opsonisation [5, 6]. Similarly, IgE is a monomeric antibody [5, 6] that is produced during a type I hypersensitivity reaction [5]. IgA is primarily found in mucosal membranes and secreted bodily fluids such as tears, saliva, and breast milk, where it exists largely as a dimer. In contrast, the majority of serum IgA is monomeric, comprising approximately 80–90% of circulating IgA [5]. Less is known about IgD compared to the other antibody isotypes, though it is believed to be important in lymphocyte differentiation [6].

These antibodies play important roles in the defence against pathogens like bacteria, viruses, and fungi. The formation of immune complexes hinges on the multivalent binding of antibodies to target antigens.

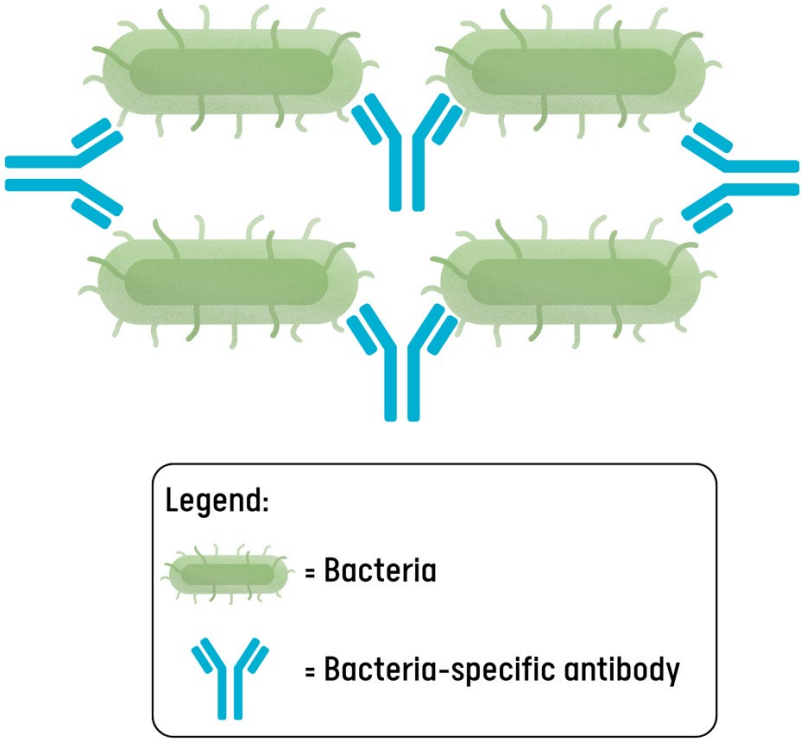

Figure 1: Bivalent IgG antibodies binding to bacterial pathogen forming an immune complex. Figure kindly provided by Ms Rachel Chea, Department of Microbiology and Immunology, National University of Singapore

III. Implications in Blood Transfusion

The ABO and Rhesus (Rh) antigens are key determining factors of a person's blood type. This blood group system is particularly important in ensuring compatibility during blood transfusion. Transfusion of incompatible blood may result in the activation of the recipient's immune response against the mismatched donor blood cells. This may lead to haemolytic transfusion reaction and shock in the recipient, and may result in death [2]. This highlights the importance of proper blood typing in a clinical setting.

Similarly, the binding of specific antibodies to antigens results in the formation of clumps or agglutination. This phenomenon is a result of cross-linking multivalent antigens and antibody molecules. In the ABO system, there are four different blood groups: A, B, AB, and O. This blood grouping is determined by the antigen present on the red blood cell (RBC) surface of a person. Essentially, Type A individuals have the A antigen on their RBC surface, Type B individuals have the B antigen, Type AB individuals have both A and B, and Type O individuals have neither antigens on their RBC surface. Additionally, every individual would not have antibodies against their own RBC surface antigens but have antibodies against the antigens that are **not** expressed on their own RBCs. For example, a Type A individual would have anti-B antibodies, while a Type B individual would have anti-A antibodies. Type AB individuals (colloquially known as the "universal recipients") would not have antibodies targeting either antigens and Type O individuals ("universal donors") would have both anti-A and anti-B antibodies [7].

In a blood banking facility, RBCs are often typed by mixing with antisera containing high titres of antibodies that bind to either antigen A or B. The presence of agglutination indicates the antigens present on the RBC surface of the blood sample [8].

A

Blood Group	Surface Antigen	Antibodies present in plasma	Compatible blood group
A	Antigen-A	Anti-B	Type A Type O
B	Antigen-B	Anti-A	Type B Type O
AB	Antigen-A Antigen-B	None	Type A Type B Type AB
O	None	Anti-A Anti-B	Type O

B

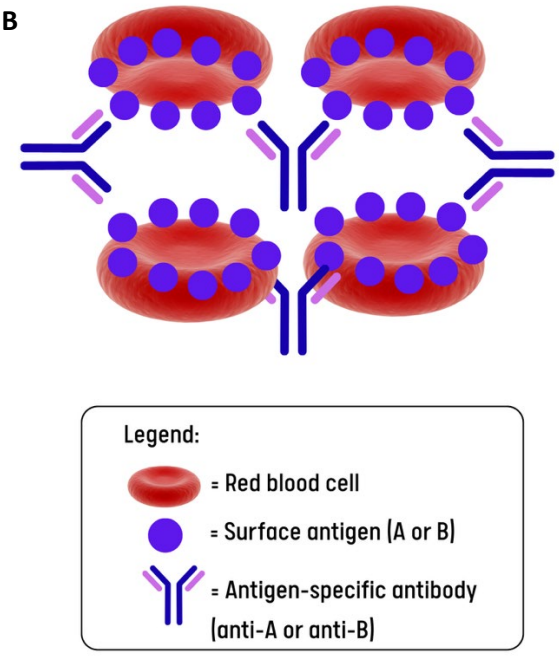

Figure 2: (A) Blood grouping and phenotype of individuals of the respective blood types. **(B)** Haemagglutination between red blood cells and specific antibodies that target the surface antigens. Table and figure kindly provided by Ms Rachel Chea, Department of Microbiology and Immunology, National University of Singapore

IV. Implications in Autoimmunity

Rheumatoid factors (RF) are a group of autoantibodies (usually IgM autoantibodies; rarely IgG or IgA) that target the Fc fragment of a patient's own IgG antibodies. This clinical feature is typical of a condition known as rheumatoid arthritis (RA) [9]. However, it is important to note that RF may also be associated with other chronic inflammatory diseases such as systemic lupus erythematosus, systemic sclerosis, leprosy, and even tuberculosis [10, 11].

In a clinical laboratory, diagnostic tests usually involve the use of a commercial test kit that aids in the detection of RFs in a patient's blood sample. These test kits contain latex beads coated with an autoantigen (human IgG) and a positive result is usually indicated by the presence of agglutination of the latex beads [12, 13].

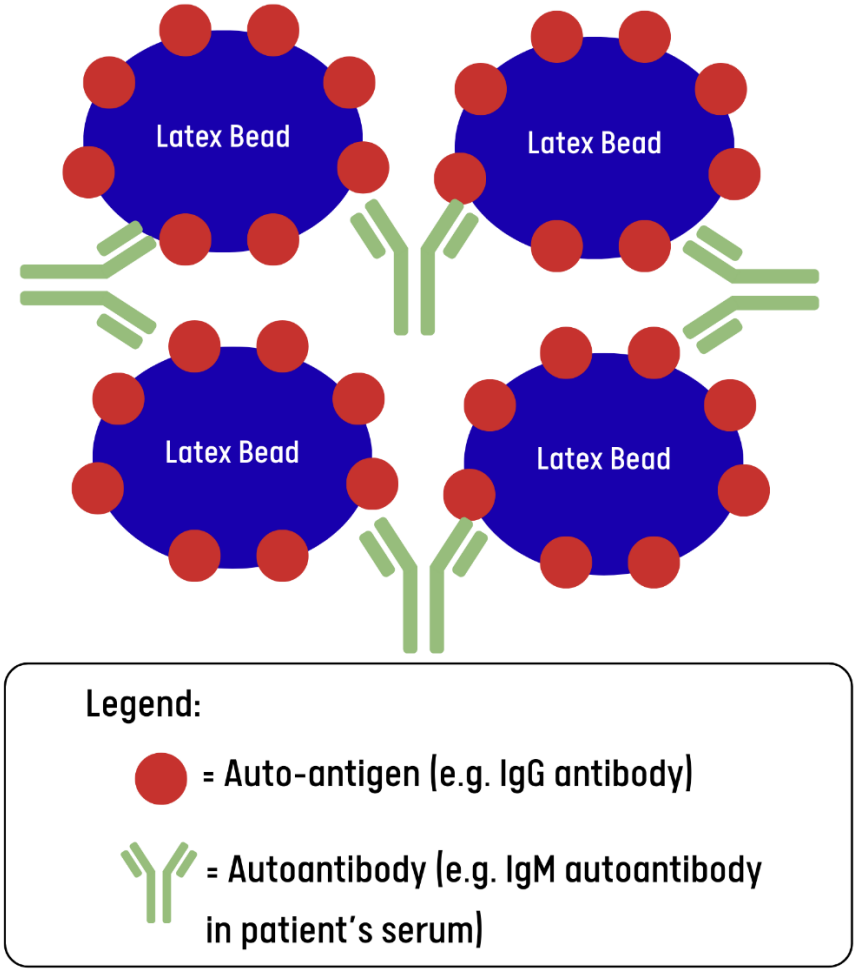

Figure 3: Schematic of the commercial latex agglutination test to detect RFs [13]. Figure kindly provided by Ms Rachel Chea, Department of Microbiology and Immunology, National University of Singapore

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